January 12, 2020

To: The Office of the Attorney General of Vermont

Via: Electronic Mail at AGO.highcostprescriptiondrugs@vermont.gov

Re: Notice of New Drug Introduction Pursuant to 18.V.S.A. § 4637(c)

Alnylam Pharmaceuticals, Inc. (Alnylam) hereby submits to the Attorney General of Vermont information regarding a new prescription drug pursuant to 18 V.S.A. § 4637. 18 V.S.A. § 4637(c) requires prescription drug manufacturers to provide the following information no later than thirty (30) calendar days after providing notification pursuant to 18 V.S.A. 4637(b) of releasing a drug into the commercial market whose wholesale acquisition cost (WAC) exceeds the threshold set for a speciality drug under the Medicare Part D Program.

18 V.S.A. §4637 does not currently define "release of the drug in the commercial market" and Alnylam is not aware of any guidance issued by the Office or any Vermont regulation that defines "release of the drug in the commercial market" for the purpose of 18 V.S.A. §4637. As a result, for the purposes of compliance with 18 V.S.A. § 4637, Alnylam considers a drug to be "release[d] . . . in the commercial market" when Alnylam makes product available for shipment to its Wholesalers, Specialty Pharmacies and other customers who purchase directly from Alnylam.

As authorized by 18 V.S.A. §4637(d), this disclosure contains only information that Alnylam has identified as being in the public domain or publicly available.

GIVLAARI™ (givosiran) is an aminolevulinate synthase 1-directed small interfering RNA indicated for the treatment of adults with acute hepatic porphyria (AHP).[1] For additional information about GIVLAARI, please see the full Prescribing Informaion, available at www.givlaari.com.

NAME OF PRESCRIPTION DRUG	NDC NUMBER	DATE OF COMMERCIAL AVAILABILITY
GIVLAARI™ (givosiran) (189 mg/ml single dose vial)	71336-1001-01	December 12, 2019

[1] GIVLAARI Prescribing Information, Revised 11/2019

(1) A DESCRIPTION OF THE MARKETING AND PRICING PLANS USED IN THE LAUNCH OF THE NEW DRUG IN THE UNITED STATES AND INTERNATIONALLY [2, 3, 4]

A. MARKETING PLAN IN THE U.S.

i. GIVLAARI will be marketed to healthcare professionals for the treatment of adults with acute hepatic porphyria (AHP) by a team of field-based sales professionals and its expenditures will include spending on the following areas.

ii. Alnylam has announced a U.S. gastrointestinal (GI) disease education and promotional agreement for GIVLAARI with Ironwood Pharmaceuticals, Inc., a GI healthcare company. Under the agreement, Alnylam will leverage Ironwood's leading capabilities in GI to promote GIVLAARI to certain healthcare practitioners, augmenting Alnylam's commercialization activities.

iii. GIVLAARI is currently being reviewed under accelerated assessment by the European Medicines Agency (EMA) for the treatment of patients with AHP, after receiving Priority Medicines (PRIME) Designation and Orphan Drug Designation from the EMA. Alnylam has also filed for marketing authorization in Brazil and intends to file in Japan and other countries in 2020.

iv. Alnylam's marketing initiatives will focus on raising awareness of the ultra-rare disease acute hepatic porphyria (AHP) and supporting the launch of GIVLAARI and may include multiple comprehensive education and training initiatives that will be provided by Alnylam's and Ironwood's employees. Examples include the development of websites, webcasts and other digital media on the disease state AHP as well as GIVLAARI. In addition, Alnylam anticipates that it will participate at scientific meetings attended by Healthcare Providers (HCPs) and may engage with HCPs through booth attendance at scientific meetings, printed materials, speaker programs and one on one meetings.

B. PRICING PLAN IN THE U.S.

When determining the price for GIVLAARI, the following factors influenced our decision-making:

i. Treatment Effect

GIVLAARI has the potential to substantially benefit patients' quality of life by reducing the frequency of AHP attacks by >70% compared to placebo.

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[2] Alnylam Announces Approval of GIVLAARI™ (givosiran) by the U.S. Food and Drug Administration (FDA) – November 20, 2019

[3] Alnylam Pharmaceuticals Conference Call to Discuss FDA Approval of GIVLAARI (Givosiran) – November 20, 2019

[4] Alnylam Announces New and Enhanced Framework for Value-Based Agreements to Accelerate Patient and Provider Access to GIVLAARI™ (givosiran) – November 20, 2019

ii. Potential to Offset Other Healthcare Costs

In the absence of GIVLAARI, an AHP patient can cost $400,000 - $650,000 annually for treatment of attacks, including hospitalization, hemin administration, and other medical interventions. GIVLAARI has been shown to reduce the frequency of attacks thereby providing the potential to reduce or avoid the costs of hospitalization and other interventions.

Alnylam is estimating that the annual average effective net price will be $442,000 based on the average weight-based monthly does of 1.2 vials per patient in the ENVISION study and before mandatory rebates to government institutions. Price may vary per individual insurance coverage and dosing.

iii. Ultra-Rare Patient Population

GIVLAARI is an RNAi therapeutic for the adult portion of a population of approximately 3,000 AHP patients with diagnosed, active disease in the U.S. and Europe.

iv. Existing Treatments Are Limited - Unmet Need

GIVLAARI is a first-of-its-kind FDA-approved therapy available in the U.S. for the treatment of adults with AHP.

v. Innovative Pricing - Value Based Agreements

Alnylam has announced a framework for value-based agreements (VBAs) designed to help patients with AHP gain access to GIVLAARI. Under this innovative framework for VBAs, participating government and commercial payers will pay the full value for GIVLAARI only when it delivers patient outcomes in the real-world setting similar to results demonstrated in clinical trials. An additional and newly designed Prevalence-Based Adjustment (PBA) feature will trigger rebates to participating payers if the number of diagnosed patients they cover exceeds current epidemiologic estimates for AHP. There are often uncertainties in diagnosis rates and disease prevalence estimates in ultra-rare diseases, making it challenging for payers to predict the number of patients who will be covered within their plans. This innovative approach offers greater certainty to payers that their overall financial risk will be adjusted if a substantially larger number of patients than currently estimated are identified, diagnosed, and treated with GIVLAARI.

vi. Alnylam's Patient Access Philosophy

Alnylam's VBA framework for ultra-rare diseases such as AHP builds upon Alnylam's Patient Access Philosophy. As part of Alnylam's Access Philosophy, the Company commits to not increase the price of GIVLAARI by more than the consumer price index for urban consumers (CPI-U), a measure of inflation, in the absence of significant investment associated with a meaningful label expansion. Commercially insured patients are expected to have little-to-no out-of-pocket costs for GIVLAARI.

(2) THE ESTIMATED VOLUME OF PATIENTS WHO MAY BE PRESCRIBED THE DRUG[5]

Currently, the population of AHP patients with diagnosed, active disease in the U.S. and Europe is estimated to be approximately 3,000.

(3) BREAKTHROUGH THERAPY DESIGNATION OR PRIORITY RVIEW BY FDA[6]

GIVLAARI was reviewed by the FDA under Priority Review and had previously been granted Breakthrough Therapy and Orphan Drug Designations in the U.S.

(4) DATE AND PRICE OF ACQUISITION, IF THE DRUG WAS NOT DEVELOPED BY THE MANUFACTURER

GIVLAARI was developed by Alnylam Pharmaceuticals.

Alnylam provides this report consistent with its good faith understanding and interpretation of 18 V.S.A. § 4637 and its provisions. In providing this report, Alnylam does not waive any rights, claims, or legal challenges with respect to 18.V.S.A. § 4637 and related legislation (including but not limited to Act 193 of 2018) or any implementing regulations thereof.

Sincerely,

Lisa Kiniklis
Director, Government Pricing & Reporting
Alnylam Pharmaceuticals

[5] Alnylam Pharmaceuticals Conference Call to Discuss FDA Approval of GIVLAARI (Givosiran) – November 20, 2019

[6] Alnylam Announces Approval of GIVLAARI™ (givosiran) by the U.S. Food and Drug Administration (FDA) – November 20, 2019